

REMARKS

The invention relates *inter alia* to synthesis of L-2-amino-4-(hydroxymethylphosphinyl) butyric acid (L-phosphinothricin, L-PPT) from 4-(hydroxymethylphosphinyl)-2-oxobutyric acid (HMPB, PPO) by enzymatic transamination with PPO-specific aspartate transaminase (Asp-TA). It is believed that no further fee is required for consideration of this Amendment. If, however, an additional fee is due, the Assistant Commissioner is authorized to charge such fee, or credit any overpayment, to Deposit Account 50-0320.

Claims 14-26 were pending in this application. In response to the restriction requirement, Applicants elected Group I, claims 14-22 with traverse. The restriction was maintained and claims 23-26 were withdrawn from further consideration by the Examiner as being drawn to a non-elected invention. In order to advance prosecution, Applicants cancel the claims drawn to non-elected subject matter without prejudice, admission, surrender of subject matter or intention of creating estoppel as to equivalents. Applicants expressly reserve the right to file divisional applications directed to the cancelled subject matter. Accordingly, claims 14-22 are now pending in this application.

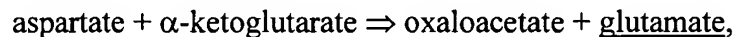
Claims 17-22 are objected to under 37 C.F.R. § 1.75 (c) as allegedly being in improper form. The amendments to the claims render the objections moot. Consequently, reconsideration and withdrawal of the objections to the claims are respectfully requested. As the amendments are formal in nature and do not narrow the scope of the claims, the application of the doctrine of equivalents is not affected.

Claims 14-15 stand rejected under 35 U.S.C. 102(b/e) as allegedly anticipated by Bartsch et al. (U.S. 6, 335, 186, "Bartsch"). Since Bartsch does not teach enzymatic transamination with

PPO-specific aspartate transaminase and employs a coupled 2-enzyme system, it cannot anticipate the present claims and the withdrawal of the rejection is requested.

The Office Action states that Bartsch “anticipate the preparation of the L-PPT” (Office Action page 4). Applicants respectfully disagree.

Bartsch relates to the production of L-phosphinothricin production by an enzymatic reaction that clearly requires the employment of 2 different enzymes. The first of these enzymes must be a GOT (glutamate/oxaloacetate-transaminase, named transaminase 1), which performs the first reaction. The reaction is summarized as follows:

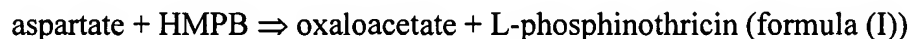


The second reaction involves a second transaminase named transaminase 2. This second reaction is summarized as follows:



(see Bartsch, column 2).

In contrast, the present invention (see page 2, line 38, continuing at page 3, line 19 of the specification) requires the enzymatic reaction to take place in the presence of only one class of enzyme (i.e. PPO-specific aspartate transaminase(s) (Asp-TA)). The reaction is summarized as follows:



Thus, it is clear that the enzymatic process of the instant invention is clearly different from the one described in Bartsch. In fact, the instant specification teaches the benefit of employing enzymes other but GOT enzymes. On page 2, lines 32-35, the specification states:

Although previously disclosed aspartate transaminases such as, for example, GOT show no conversion of PPO, aspartate transaminases from microorganisms which likewise accept L-PPT/PPO with high specificity as substrate have now surprisingly been found.

(see also page 2, lines 32-36 of the specification).

Accordingly, in view of the foregoing, Bartsch cannot anticipate the present claims. As discussed above, Bartsch employs a coupled 2-enzyme system. The present invention employs one class of enzymes which are completely different. Accordingly, Bartsch does not meet each and every element of the invention as claimed and therefore cannot anticipate the present claims. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Claims 14 to 16 stand rejected under 35 U.S.C. 112, first paragraph, for allegedly lacking enablement. For the reasons that follow, Applicants respectfully assert that the specification in combination with the knowledge in the art, discloses sufficient information about the microorganisms used to obtain specific enzymes and about the source of specific enzymes used in the instant transamination reactions, and thus fully enables one to make and use the invention without undue experimentation. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

The Office Action asserts that “one of ordinary skill in the art cannot make and use the specific enzyme without the required microorganism or sufficient information pertaining to the structure of the enzyme per se” (Office Action page 5). Further, the Office Action states that “the instant specification does not provide information as to the specific microorganism(s) to obtain the specific enzymes”. *Id.* Applicants respectfully disagree. Applicants respectfully urge that the specification taken together with the knowledge in the art provides adequate guidance to the skilled artisan to make and use the specific enzymes. Moreover, the Examiner is respectfully

reminded that the first paragraph of 35 U.S.C. § 112 requires nothing more than objective enablement. Whether this is achieved by illustrative examples or by broad terminology is of no importance. *In re Marzocchi*, 169 U.S.P.Q. 367 (CCPA 1971).

The instant invention describes the use Diversa enzymes with required specific activity (Diversa Corporation, 4955 Directors Place, San Diego, CA 92121-1609), AMN-001-03 and AMN-001-04, for the in instant transamination reactions (see specification line 22-25 at page 9, Example 2). From these two, AMN-001-03, was chosen to be employed for further characterization (see Examples 3 and 4). These two enzymes are commercially available from Diversa Corporation, a company well known within the scientific community as a commercial source of transamination enzymes, and are well characterized in terms of structure and function. The company name as well as the catalogue number are given in the specification at page 9, lines 6-9.

Further, Example 1 clearly describes the details of the procedure for the identification and isolation of soil organisms with L-PPT-specific aspartate transaminase activity. Based on such an assay system, 4 strains have been isolated from which a sample (DSM 13353-13356; see cancelled claims 23-26 and specification at page 7, lines 17-19) has been deposited (in accordance with the Budapest Treaty) at the “Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH” (see specification at 7, lines 17-19). Finally, one skilled in the art may use the experimental setup described in Example 1 for the isolation of further soil microorganisms expressing a transaminase of the biochemical properties required for the instant transamination reactions. Hence, the specification in the light of the current knowledge of the art provides sufficient information to one skilled in the art pertaining to the structure of the PPO-specific aspartate transaminase and to the specific microorganisms used to obtain PPO-specific

transaminases. Thus, in view of the foregoing, it is respectfully submitted that the teachings in the specification, in combination with the knowledge in the art, invention and fully enable one skilled in the art to make and use the claimed invention. Accordingly, it is respectfully requested that the Section 112, first paragraph, rejections be reconsidered and withdrawn.

Claims 14 to 16 stand rejected under Section 112, first paragraph, for allegedly not setting forth the best mode to practice the invention. Applicants respectively disagree.

First, Applicants urge that it is not the function of the claims to set forth the best mode, but rather the specification. Hence, it is urged that the rejection is improperly raised.

Second, the Examiner is reminded that the issue of best mode determined on the subjective intent of the inventors at the time the invention was filed and that U.S. patent law does not require a specific identification of what constitutes best mode on the specification.

Applicants further assert that the specification contains the best mode for practicing the invention known to them at the time the application was filed.

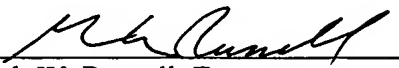
Finally, it appears that this rejection is based on the allegation that the “enzyme(s) required to practice the invention” are not enabled by the specification and concludes that “this lack of information may be considered to be evidence of concealment of best mode.” Office Action at 5. For the reasons presented above, Applicants submit that the specification does adequately enable the enzymes used to practice the invention and thus the rationale behind the rejection is invalid. Accordingly, the withdrawal of this rejection is requested.

Favorable action is earnestly solicited.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP
Attorneys for Applicants

By:



Mark W. Russell, Esq.
Registration No. 32,517
745 Fifth Avenue
New York, New York 10151
(212) 588-0800